DETAILED ACTION

Claims 1-9, 12-13, 15-25 and 27-29 are presented for examination.

Applicant's Amendment filed September 15, 2009 has been received and entered into the present application.

Claims 1-9, 12-13, 15-25 and 27-29 remain pending and under examination. Claims 11 and 30-33 are cancelled. Claims 1, 12-13 and 22 are amended.

Applicant's remarks, filed September 15, 2009, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Objection to the Claims (New Grounds of Objection)

Claims 3-4 and 24-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In particular, the administration scenarios circumscribed by the limitations of instant claims 5-9 directly conflict with the embodiments provided for in instant claim 1 and, as a result, render the claims indefinite. Specifically, instant claim 1 clearly provides for the treatment of alopecia in a patient *prior to*

exposure to radiation for a time and at an intensity sufficient to result in alopecia, i.e., the patient is to be treated prior to radiation exposure and, therefore, at the time of treatment (i.e., via oral or parenteral administration of the methionine protective agent), has not been exposed to radiation. However, instant claims 5-9 clearly circumscribe administration of the methionine protective agent *after radiation exposure*, which is, at least with regard to the embodiment wherein the patient is treated prior to radiation exposure, an administration scenario that is impossible to execute. In other words, it would be impossible to administer the claimed methionine agent after radiation exposure in a patient that has not been exposed to radiation.

Similarly, instant claim 1 also clearly provides for the treatment of alopecia in a patient *simultaneously with or subsequent to exposure to radiation for a time and at intensity sufficient to result in alopecia*. However, instant claims 5-9 clearly circumscribe administration of the methionine protective agent *prior to radiation exposure*, which is, at least with regard to the embodiments wherein the patient is treated simultaneously with or subsequent to radiation, an administration scenario that is impossible to execute. In other words, it would be impossible to administer the claimed methionine agent prior to radiation exposure if the administration of the claimed protective agent occurs simultaneously with or subsequent to exposure to radiation. As a result, one of ordinary skill in the art would not have been reasonably apprised of the metes and bounds of the subject matter for which Applicant is presently seeking protection. Clarification is required.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claim Rejections - 35 USC § 102 (New Grounds of Rejection)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5-9 and 12-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Dye (U.S. Patent No. 5,122,369; 1992, already of record).

Dye teaches a nutrient composition for decreasing the rate of hair loss via the daily consumption of an orally acceptable composition (col.2, l.44-52) comprising d,l-methionine, pantothenic acid and divalent iron in an amount sufficient to effect reduction of the rate of hair loss (col.2, l.65-68). Dye further teaches that d,l-methionine is present in an amount sufficient to effect reduction of the rate of hair loss (col.2, l.47-52).

The teaching of d,l-methionine meets Applicant's limitations of present claims 12-13, which provide for the use of d-methionine or l-methionine, since by the very nature of the d,l-methionine mixture, both the d-isomer and the l-isomer are present.

Note that present claim 1 is directed to a "method for treating alopecia in a patient prior to" exposure to radiation for a time and at an intensity sufficient to result in alopecia, which is met by the teachings of Dye, whose discloses the oral administration of an effective amount of a d,l-methionine composition to a patient with hair loss (i.e., alopecia) to reduce the rate of hair loss. Though it is acknowledged that Dye does not specifically teach that the alopecia results from exposure to radiation for a time and at an intensity sufficient to cause hair loss, the embodiment of the claims wherein the treatment occurs "prior to" radiation exposure is clearly indicative of the fact that the patient to be treated in this embodiment has not yet been exposed to the radiation. In other words, the instant claims clearly read upon the treatment of alopecia in a patient that has not yet been exposed to radiation (as evidenced by the phrase "a patient prior to…exposure to radiation") and, thus, are clearly met by the teachings of Dye, who teaches the treatment of alopecia in a patient via oral administration of a composition comprising an effective amount of d,l-methionine. In addition, because the patient is not required by the instant claims

to have been exposed to radiation, the limitations of instant claims 5-9 directed to the administration of the effective amount of the protective methionine agent relative to the point at which the patient is exposed to radiation are also met by the teachings of Dye because the patient to be treated is administered the methionine prior to any exposure to radiation and, therefore, is considered to be within the claimed time periods occurring before the patient may be exposed to radiation, absent factual evidence to the contrary.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 5-9, 12-13, 15-23 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dye (U.S. Patent No. 5,122,369; 1992) in view of Remington's Pharmaceutical Sciences (p.702-703; 1975).

All references are already of record.

Dye teaches a nutrient composition for decreasing the rate of hair loss via the daily consumption of an orally acceptable composition (col.2, l.44-52) comprising d,l-methionine, pantothenic acid and divalent iron in an amount sufficient to effect reduction of the rate of hair loss (col.2, l.65-68). Dye further teaches that d,l-methionine is present in an amount sufficient to effect reduction of the rate of hair loss (col.2, l.47-52).

The teaching of d,l-methionine meets Applicant's limitations of present claims 12-13, which provide for the use of d-methionine or l-methionine, since by the very nature of the d,l-methionine mixture, both the d-isomer and the l-isomer are present.

Note that present claim 1 is directed to a "method for treating alopecia in a patient prior to" exposure to radiation for a time and at an intensity sufficient to result in alopecia, which is met by the teachings of Dye, whose discloses the oral administration of an effective amount of a d,l-methionine composition to a patient with hair loss (i.e., alopecia) to reduce the rate of hair loss. Though it is acknowledged that Dye does not specifically teach that the alopecia results from exposure to radiation for a time and at an intensity sufficient to cause hair loss, the embodiment of the claims wherein the treatment occurs "prior to" radiation exposure is clearly indicative of the fact that the patient to be treated in this embodiment has not yet been exposed to the radiation. In other words, the instant claims clearly read upon the treatment of alopecia in a patient that has not yet been exposed to radiation (as evidenced by the phrase "a patient prior to…exposure to radiation") and, thus, are clearly met by the teachings of Dye, who teaches the treatment of alopecia in a patient via oral administration of a composition comprising an effective amount of d,l-methionine. In addition, because the patient is not required by the instant claims to have been exposed to radiation, the limitations of instant claims 5-9 directed to the administration of the effective amount of the protective methionine agent relative to the point at which the patient is exposed to radiation are also met by the teachings of Dye because the patient to be treated is administered the methionine prior to any exposure to radiation and, therefore, is considered to be within the claimed time periods occurring before the patient may be exposed to radiation, absent factual evidence to the contrary.

Dye fails to teach (1) wherein the administration of the effective amount results in a blood serum level equivalent to that achieved by parenteral administration of from 1.0-600 mg/kg body weight (claims 15 and 22), 5-500 mg/kg body weight (claim 16) or 10-400 mg/kg body weight (claim 17), (2) further administering a supplemental amount of the methionine agent after administration of the effective amount (claims 18 and 27), (3) wherein the administration of the supplemental amount is sufficient to maintain an effective blood serum level of the agent in the patient for a period of from 1-14 days after administration

of the effective amount (claims 20 and 28), or (4) wherein the administration of the supplemental amount is sufficient to maintain a blood serum level of at least 10% of the blood serum level achieved by administration of the effective amount (claims 21 and 29).

Regarding the limitation(s) directed to (1) wherein the administration of the effective amount results in a blood serum level equivalent to that achieved by parenteral administration of from 1.0-600 mg/kg body weight (claims 15 and 22), 5-500 mg/kg body weight (claim 16) or 10-400 mg/kg body weight (claim 17), the determination of the optimum dosage regimen and schedule of administration to treat alopecia with the presently claimed active agent would have been a matter well within the purview of one of ordinary skill in the art. Such a determination would have been made in accordance with a variety of factors, such as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage regimen and schedule of administration that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific dosage amounts and schedule of administration are not seen to be inconsistent with that which would have been determined by, and well within the routine skill of, the skilled artisan.

In addition, the concentration of the active ingredient is a result-effective variable, i.e., a variable that achieves a recognized result, and, therefore, the determination of the optimum workable range would be well within the practice of routine experimentation by the skilled artisan, absent factual evidence to the contrary and, further, absent any evidence demonstrating a patentable difference between the compositions used and the criticality of the amount(s). As taught by the MPEP at §2144.05, "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Regarding the limitations directed to (2) further administering a supplemental amount of the methionine agent after administration of the effective amount (claims 18 and 27) and (3) wherein the administration of the supplemental amount is sufficient to maintain an effective blood serum level of the agent in the patient for a period of from 1-14 days after administration of the effective amount (claims 20 and 28), one of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to administer a supplemental amount of the d,l-methionine therapy of Dye for the purpose of treating alopecia because the methionine-containing composition was disclosed as having efficacy in ameliorating hair loss and, thus, the administration of a supplemental amount for the same purpose would have been reasonably expected to provide at least additive protective effects against hair loss as compared to a single administration of the same, absent factual evidence to the contrary. Such a person would have been motivated to do so (and, in particular, to provide an amount to the patient in need thereof sufficient to maintain an effective blood serum level of the agent for a period of from 1-14 days after administration of the first initial effective amount) in order to provide a baseline plasma concentration of the active methionine composition to provide long-term hair-protecting effects throughout the chronic process of hair loss so as to maximize hair retention. The determination of the optimum amount of time (i.e., from 1-14 days after administration of the first initial effective amount) over which to maintain an effective blood serum level of the agent would depend upon a variety of factors, including the extent of hair loss, the progression of the severity of the hair loss, and whether other concomitant therapies were also being used to encourage hair retention. As a result, the amount sufficient to maintain an effective blood serum level for a period of from 1-14 days that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed amount necessary to provide an effective amount for 1-14 days after administration of the first initial effective amount would not have been inconsistent with that which would have been determined by the skilled artisan, absent factual evidence to the contrary.

Remington's Pharmaceutical Sciences teaches that multiple dose administration may be used when the duration of therapy exceeds the effective sojourn of the drug in the body when used as a single administration (p.702). Remington's further teaches that, for multiple dose administrations, a dose is used wherein the plasma concentration rises to a maximum (C_{max}) after each administration and falls to a minimum (C_{min}) (p.702) such that the dosage interval effectively reaches a plateau wherein the absorption, distribution and elimination have reached a fluctuating steady state concentration (p.702).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to administer the supplemental dose of the complex in an amount sufficient to maintain a blood serum level of at least 10% of the blood serum level achieved by administration of the initial effective amount because the skilled artisan would have been motivated to administer a dosage effective to provide a rate of absorption, distribution and elimination that was essentially equivalent so as to result in a steady state plasma concentration during multiple dosing (i.e., the initial effective amount as disclosed by Dye plus the subsequent supplemental amount). Such a person would have been motivated to do so in order to provide a plasma concentration of the active agent that is effective to achieve the claimed purpose of treating alopecia while accounting for the body's natural rate of distribution and elimination of the active agent so as to maintain a steady state plasma concentration of the active agent, absent factual evidence to the contrary.

Conclusion

Rejection of claims 1-2, 5-9, 12-13, 15-23 and 27-29 is proper.

Claims 3-4 and 24-25 are objected to for depending from a rejected base claim.

No claims of the present application are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
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January 14, 2010

/Ardin Marschel/
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